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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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CORPORATE INTELLECTUAL PROPERTY
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EXAMINER	
BASQUILL, SEAN M	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,946	AUKUNURU ET AL.	
	Examiner	Art Unit	
	Sean Basquill	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-34,37-39 and 42-53* is/are pending in the application.

4a) Of the above claim(s) *44 and 50-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-34,37-39,42,43 and 45-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *16 Sep 2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Previous Rejections

1. Applicants' arguments, filed 16 September 2009, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of the Claims

2. Claims 28, 34, and 37-39 have been amended, Claims 1-27, 35, 36, 40, and 41 have been cancelled. Claims 44 and 50-53 are withdrawn as directed to a nonelected invention. Claims 28-34, 37-39, 42, 43, and 45-49 are presented for examination.

Claim Rejections - 35 USC § 112 First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 28-34, 37-39, 42, 43 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, as put forth in the previous office action.

Applicants arguments have been fully considered and are deemed unpersuasive. As applicants are aware, it is inappropriate to import limitations from the specification into a claim when construing the meaning and breadth of same. MPEP 2111.01(II). While it may be true that certain types of derivatives of staurosporine may have been adequately described to survive analysis under 35 USC 112, first paragraph, the instant claim is not limited to these types of staurosporine derivatives. The instant claims read on any possible chemical compound which may be considered a derivative of staurosporine by the skilled artisan, and in the support of this claim applicants fail.

Claim Rejections - 35 USC § 112 Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 43 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As put forth previously, the term "derivative" is indefinite because it is unclear how far one can deviate from the parent compound without the "derivative" being so far removed therefrom as to be a completely different compound.

Applicants arguments have been fully considered and are deemed unpersuasive for the reasons put forth in the examiner's response concerning the inadequate written description provided for the term "derivative."

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 28-34, 37-39, 42, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 6,107,343 ("Sallmann").

Sallmann discloses an eye ointment for the delivery of ophthalmically effective active agents containing phenylethyl alcohol (5%) as a preservative, cetylstearyl alcohol (2.2%), liquid paraffin (2.07%), white petrolatum (4.62%) and wool fat (14.15%) described above. Sallmann also indicates that topical ophthalmic compositions can include solubilizers such as polyethylene glycols and polyethoxylated castor oils such as Cremophor EL in concentrations of between 0.1-5000 times that of the active agent. (C.4, L.52-67). Specifically, PEG 400 is listed as one of the polyethylene glycols usable in the instant invention. (C.5, L.45-46).

The specific combination of features claimed is disclosed within the broad generic ranges taught by the reference but such "picking and choosing" within several variables does not necessarily give rise to anticipation. *Corning Glass Works v. Sumitomo Elec.*, 868 F.2d 1251, 1262 (Fed. Circ. 1989). Where, as here, the reference does not provide any motivation to select this specific combination of solubilizers and fillers, anticipation cannot be found.

That being said, however, it must be remembered that "[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR v. Teleflex*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. A.G. Pro*, 425 U.S. 273, 282 (1976)). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious", the relevant question is "whether the improvement is more than the predictable use of

prior art elements according to their established functions." (*Id.*). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR v. Teleflex*, 127 S.Ct. 1727, 1741 (2007). The Court emphasized that "[a] person of ordinary skill is… a person of ordinary creativity, not an automaton." *Id.* at 1742.

Consistent with this reasoning, it would have obvious to have selected various combinations of various disclosed solubilizers and fillers from within Sallmann, to arrive at compositions "yielding no more than one would expect from such an arrangement."

Applicants arguments have been fully considered and are deemed unpersuasive. While under different circumstances, the fact that one embodiment chosen from among a prodigious list may not give rise to obviousness, such circumstances are not present here. See In re Baird, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994) (indicating that a claimed compound being encompassed by a disclosed generic formula, along with approximately 100 million others, does not give rise to a legal conclusion of obviousness). The facts of Baird and related cases simply does not apply here. The motivation to select polyethylene glycol is provided by the disclosure of Sallman itself, which indicates that the claimed polyethylene glycols are known and commonly used in ophthalmic compositions to provide the precise utility relied upon by the applicants here. Caution must be exer4cised in granting a patent on a combination of elements known in the prior art which perform no more than their expected function. *KSR International Co. v. Teleflex, Inc.* 82 USPQ2d 1385, 1395 (U.S. 2007). It is *prima facie* obvious to select a known material for incorporation into a composition, based on its recognized suitability for its intended use. MPEP

2144.07. Where, as here, applicants have advanced no evidence of unexpected results obtained through the use of polyethylene glycols in ophthalmic compositions, the obviousness rejection will stand.

6. Claims 28-34, 37-39, 42, 43 and 45-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sallmann as applied to claims 28-34, 37-39, 42, and 47 above, and further in view of U.S. Patent 5,093,330 ("Caravatti").

Sallmann discloses an eye ointment containing phenylethyl alcohol (0.5%) as a preservative, cetylstearyl alcohol (2.2%), liquid paraffin (2.07%), white petrolatum (4.62%) and wool fat (14.15%) described above. Sallmann also indicates that topical ophthalmic compositions can include solubilizers such as polyethylene glycols and polyethoxylated castor oils such as Cremophor EL. Specifically, PEG 400 is listed as one of the polyethylene glycols usable in the instant invention. The particular eye ointments described by Sallmann are for the delivery of drugs to treat ocular inflammatory disorders and all ophthalmological disorders involving inflammatory processes. (C.3, L.27-30).

Sallmann does not specify the inclusion of staurosporine derivatives, particularly midostaurin, in compositions for the treatment of inflammatory ocular disorders.

Caravatti describes the use of staurosporine derivatives, particularly midostaurin (Example 18, C.28, L.45-57; C.2, L.40 – C.3, L.5; C.3, L.57), in compositions for the treatment of diseases modulated by protein kinase C, including use as an immunomodulator or antiinflammatory. (C.2, L.18-50).

It would have been prima facie obvious to one having ordinary skill in the art at the time of the instant invention to have used antiinflammatory staurosporine derivatives, particularly midostaurin described by Caravatti in the topical ophthalmic composition described by Sallmann. One having ordinary skill in the art at the time of the instant invention would have been motivated to use midostaurin in the composition of Sallmann because the art recognized the antiinflammatory properties of midostaurin, as well as the use of the composition of Sallmann in delivering ocular antiinflammatory agents. The combination of the two simply represents the combination of elements known by the art as suitable for their intended purpose.

Neither Sallmann nor Caravatti describes the precise concentrations of all ingredients as taught in instant Claim 49, however, the combination of Sallmann and Caravatti does disclose the general conditions of the concentrations of each element of the composition as claimed.

Where the general conditions of a claim are known via the prior art, it is not inventive to discover optimum or workable concentration ranges by the routine experimentation of one having ordinary skill in the art, absent evidence presented indicating the claimed range is critical. MPEP § 2144.05(II)(A).

Applicants arguments have been fully considered and are deemed unpersuasive. Sallman discloses ophthalmic ointments for delivery of antiinflammatory drugs; Caravati discloses that staurosporine derivatives such as midostaurin possess antiinflammatory properties. It is *prima facie* obvious to combine two compositions, each of which is taught by the prior art to be useful for same purpose, in order to form a third composition to be used for the very same purpose. The idea for combining them flows logically from their having been individually taught in the

prior art. MPEP 2144.06. Diclofenac potassium is a known antiinflammatory, as is midostaurin. In light of the prevailing precedent, the examiner's prima facie case requires nothing more.

7. Claims 28-33, 35-39, 42 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 6,579,901 ("Chen") as evidenced by U.S. Patent 3,134,718 ("Nobile") in view of U.S. Patent 4,524,075 ("Oduro"), and Shulin Ding, *Recent Developments in Ophthalmic Drug Delivery*, 1 PSTT 328 (November 1998) ("Ding").

Chen discloses eye ointments comprising in one embodiment tacrolimus, anhydrous lanolin, liquid paraffin, vaseline, and polyoxyethylated castor oil (C.3, L.50-55) and in another embodiment tacrolimus, anhydrous lanolin, liquid paraffin, vaseline, and HCO60. (C.5, L.20-50). One embodiment, example 4, contains HCO60 in a concentration of 2.29% by weight of the composition. (C.5, L.20-30). Chen additionally indicates additives such as surfactants and bacterial suppressants are incorporated into ophthalmic compositions. (C.3, L.1-9).

Nobile indicates that anhydrous lanolin and wool fat are synonymous. (C.20, L.60, 71).

Chen does not describe ophthalmic compositions comprising a polyethylene glycol, but clearly indicates that "there are many surfactants frequently used for ophthalmic purposes and all of them are suitable for this invention." (C.3, L.30-35).

Oduro describes the use of polyethylene glycols such as PEG 400 for the formation of eye ointments or eye drops of a desired consistency. (C.2, L.20-42). Oduro indicates that the chosen PEG should be present in a concentration of at least 1% by weight of the composition. (C.2, L.57-60). Oduro additionally indicates that appropriate additional conventional additives

such as preservatives may be incorporated into compositions for ocular administration, along with compatible conventional carriers like ointment bases. (C.2, L.43-47).

Ding teaches that the use of viscosity enhancers are commonly used in topical ophthalmic pharmaceuticals to prolong residence time and improve bioavailability of the active agents. (Pg. 328-29).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time of the instant invention to include a preservative and polyethylene glycol viscosity enhancer such as PEG 400 in the composition of Chen. One having ordinary skill in the art at the time of the instant invention would have been motivated to do so in order to increase the viscosity of the ophthalmic composition and improve bioavailability of the active agent without increasing the concentration of active agent in the composition.

Applicants arguments have been fully considered and are deemed unpersuasive. Applicants are reminded that art is art, not only for what it expressly teaches, but also for what it would reasonably suggest to the skilled artisan, including alternative or nonpreferred embodiments. MPEP § 2123. In formulating their rebuttal, Applicants take an improperly narrow view of the teaching of Oduro, which clearly indicates that polyethylene glycols are used to vary the consistency of pharmaceutical formulations. As such, the stabilization of pseudomonic acid is irrelevant to the examiner's motivation for the inclusion of PEG into the composition of Chen, and the examiner's rejection stands.

Conclusion

No Claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean Basquill whose telephone number is (571) 270-5862. The examiner can normally be reached on Monday through Thursday, between 8AM and 6PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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